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03/12/2004

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EXAMINER

YAO, LEI

ART UNIT

PAPER NUMBER

1642

MAIL DATE

DELIVERY MODE

07/24/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/799,797

Applicant(s)

VISVADER ET AL.

Examiner

Lei Yao, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 2,4,6,10-17,21,24-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,7-9,18-20,22,23 and 40 is/are rejected.
- 7) ☒ Claim(s) 1,3,18-20,22 and 23 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/4/2007.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Art Unit: 1642

Response to Argument and Amendment

The Amendment filed on 5/4/2007 in response to the previous Non-Final Office Action (11/2/2006) is acknowledged and has been entered.

Claims 18 and 23 are amended. Claims 1-40 are pending. Claims 2, 4, 6, 10-17, 21, 24-39 have been withdrawn previously for non-elected invention. Claims 1, 3, 5, 7-9, 18-20, 22, 23, and 40 are under consideration.

Applicant argues that claim 6 should be rejoined if the generic claims are found allowable. Based on the MPEP 821.04 (b), applicant's request is considered and held in abeyance until the generic claims are found allowable.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 5/4/2007 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Priority

1. Applicant does not further argue the priority from foreign document PR7618/01 in term of using monoclonal antibody 16H2 or 20F8, which certified copy has been submitted to the Office.
2. Submitting certified copy of parent application PCT/AU02/01246 is also acknowledged and requirement is withdrawn.

Rejections Withdrawn

1. The rejection of claims 18 and 23 under 35 U.S.C. 112, second paragraph, as being indefinite for terms "derived from" and "derived parts" is withdrawn in view of the amendments to the claims.
2. The rejection of claims 18, 20, and 23 under 35 U.S.C. 112, first paragraph, for lacks complete deposit information is withdrawn in view of receiving the receipt for patent deposit with the European collection of cell cultures and the statement of public availability in the remarks filed 8/4/2006 and applicant's argument. However, the statement of public availability is required to be recorded in the specification (see below).

Art Unit: 1642

Specification

Amendment to the specification is required to update the biological deposit information in accordance with the Budapest Treaty and statement made in the remarks (page 14) filed on 8/4/2006.

Claim Objections

Claims 1, 3, 18-20, 22, and 23 are objected to because of the following informalities: The specification provides definition of LMO family protein comprising LMO4 (page 2, line 23-28). However, the abbreviation LMO4 should be spelled out when first used in the claims. Appropriate correction is required.

Response to Arguments**Rejection under 35 USC § 112, first paragraph**

1. Claims 1, 3, 5, 7-9, 18, 22 and 23 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the claimed method of using an immunoiteractive molecule, variable antibody fragments, or an analogue etc. as stated and discussed in the previous Office actions.

The response filed 5/4/2007 has been carefully considered but is deemed not to be persuasive. Applicant on page 13 argues that "*immunointeractive*" indicates that the molecule interacts via an immunological mechanism. The generally recognized immunological mechanisms are those, which attach to antibody and T-cell receptor like interactions and which therefore require antibody-like or T-cell receptor-like molecules. Applicant also argues that it is a well known concept that antibody specificity for diagnostic or therapeutic purposes extends well beyond conventional monoclonal antibody structure to, for instance, divalent, trivalent and single chain forms that retain target specificity and provided references of generation of antibody fragments. In response to this argument, first, the claimed invention is drawn to a method of detecting the interaction of immunointeractive molecule with elevated levels of LMO4 protein in the cells to indicate the aberrant cell or cell growth. Based on the requirement under USC 112 first, the application must provide an enablement disclosure to allow one skilled in the art to practice claimed invention without undue experimentation. Although instant specification teaches that overexpression of

Art Unit: 1642

LM)4 protein in primary breast cancer is detected by rat-anti-LMO4 monoclonal antibody (fig 5, example 1), the specification neither teaches that an interaction of LMO4 overexpressed on a cell with any other molecule comprising "T-cell receptor-like molecule" stated in the remarks above could be used to detect aberrant cell or cell growth, nor identify any molecule that interacts with LMO4 protein only overexpressed on the aberrant growing cells. Specification, example 7, teaches CTIP protein interacting with LMO4 by co-immunoprecipitation from epithelial cells, but no direction/guideline, objective evidence, or nexus to show interaction between these endogenous proteins in the normal breast epithelial cells for detecting the aberrant cells or cell growth. Thus, one skilled in the art would not know how to use the interaction of LMO4 and immunointeractive molecule except antibody to practice claimed method. Moreover, applicant provided references that teach the antibody for diagnosis or therapy as well as the method of producing antibody fragment. However, one skilled in the art would not use the concept for diagnosing or treating particular disease without undue experimentation because using a particular antibody or immunointeractive molecule for diagnosing or treating a particular disease is unpredictable. Applicant has not provided such evidence or direction of using any immunointeractive molecule comprising the specific antibody, 16H2 (elected), recited in claims 20 and 23, which allow one skilled in the art to practice broadly claimed invention without further experimentation. In addition, the Office does not understand the argument about the relationship between neoplastic cell development and levels of LMO4; on page 14 line 7-10. Claimed invention is contradictory with this argument because neoplastic cell development is considered a process of aberrant cell growth. Clarification is required. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained.

2. Claims 1, 3, 18 and 23 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the antibody used in the claimed method having all CDRs as stated and discussed in the previous Office actions.

The response filed 5/4/2007 has been carefully considered but is deemed not to be persuasive. Applicant on page 15 argues that the full complement of CDRs is not required to produce a protein with the requisite antigen binding function and provide references (exhibits 6-11) to support the single domain antibodies exhibit good antigen binding affinities. In response to this argument, the issue of binding

Art Unit: 1642

antibody to its antigen has been explicitly discussed in the previous office action dated 11/2/2006 and generally the art considers that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope. The references provided by applicant teach that replacing one or more CDR(s) of one immunoglobulin with CDR(s) from an immunoglobulin may not lose the antigen binding ability, the best example is humanized mouse monoclonal antibody for the purpose of using mouse antibody for therapy. However, none of the references teaches missing one or more CDRs could maintain the same antigen binding capacity. Current specification does not teach any antibody with less than entire 6 CDR(s) could be used in the claimed method for detecting the aberrant cells or cell growth. Thus, applicant has provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of containing fewer than six CDRs that retains the antigen specificity of the parental antibodies comprising 16H2. One of skilled in the art would neither expect nor predict the appropriate functioning of the antibody broadly used as claimed. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained.

Rejection under 35 USC § 102

Claims 1, 3, 5, 7-9, 18-20, 22, 23 and 40 remain rejected under 35 U.S.C. 102(e) as being anticipated by Paml et al., (US patent application publication, 2003/0092009, effective filing date Nov 16, 2000).

The response filed 5/4/2007 has been carefully considered but is deemed not to be persuasive. Applicant on page 16 argues that *the levels of autoantibodies in a sample does not necessarily reflect the levels of the LMO4 antigen and changes in the expression levels of a self antigen is entirely independent of the generation of autoantibodies*. Applicant further argues that *there should not be an immune response by self antigen LMO*. The Office agrees with the statement about the relation between the autoantibody and antigen self, however, claimed method is drawn to a method of detecting the presence of LMO4, aberrant cells, cell growth comprising the mammal cells by elevated levels of complex of LMO4

Art Unit: 1642

protein and its immunointeractive molecule comprising the antibody in the sample. The method does not limit the immunointeractive molecule to particular type of antibody or binding domain and does not exclude an autoantibody in the method. The reference by Paml et al., teach the presence and elevated complex of *LMO4* protein and its antibodies comprising autoantibody in neoplastic mammary cells compared to the normal cells. In addition, Paml et al., teach that assay of *LMO4* in certain tumor sample, such as glioblastoma by interaction with its specific antibody (example 1, table 10). Applicant does not provide the evidence showing the difference between the antibodies in the claims and antibodies in the reference. Thus, the reference teaches every limitation of claimed method and would anticipate claimed invention. Therefore, applicant's argument has not been found persuasive, and the rejection is maintained for reason of the record.

Conclusion

NO claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1642

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,
Examiner
Art Unit 1642

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